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EXAMINER

WARDEN, JILL ALICE

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte JAMES A. LAUGHARN, JR.,
David W. Bradley, and Robert A. Hess

Appeal 2010-001827
Application 10/770,241
Technology Center 1700

Before EDWARD C. KIMLIN, LINDA M. GAUDETTE, and
MARK NAGUMO, *Administrative Patent Judges*.

NAGUMO, *Administrative Patent Judge*.

DECISION ON APPEAL¹

¹ The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, or for filing a request for rehearing, as recited in 37 C.F.R. § 41.52, begins to run from the “MAIL DATE” (paper delivery mode) or the “NOTIFICATION DATE” (electronic delivery mode) shown on the PTOL-90A cover letter attached to this decision.

A. Introduction²

James A. Laugharn, Jr., David W. Bradley, and Robert A. Hess (“Laugharn”) timely appeal under 35 U.S.C. § 134(a) from the final rejection³ of claims 1, 2, 6, 7, 9-14, and 32-37, which are all of the pending claims. We have jurisdiction under 35 U.S.C. § 6. We AFFIRM.

According to the 241 Specification, there is a need for methods to inactivate microbes and viruses from protein preparations while maintaining the integrity and therapeutic value of the proteins. (Spec. 3, ll. 14-17.) The claimed method is said to accomplish this goal by raising and lowering the pressure of the sample several times while keeping the sample temperature below 45°C.

Representative Claim 1 reads:

1. A method for sterilizing a material, the method comprising:
providing said material at an initial pressure; and
*while maintaining said material in a temperature range
that is below 45°C,*
increasing the pressure to an elevated pressure,
then

² Application 10/770,241, *Rapid Cryobaric Sterilization and Vaccine Preparation*, filed 2 February 2004, as a continuation of an application filed 7 August 2001, which is in turn a continuation-in-part of an application filed 2 October 1998, which is a continuation in part of an application filed 15 June 1998. The Specification is referred to as the “241 Specification,” and is cited as “Spec.” The real party in interest is listed as Pressure Biosciences, Inc., formerly known as Boston Biomedica, Inc. (Appeal Brief, filed 18 March 2009 (“Br.”), 3.)

³ Office action mailed 27 September 2005 (“Final Rejection”; cited as “FR”).

decreasing the pressure below the elevated pressure, and
cycling the pressure between a decreased pressure and the elevated pressure at least two times,
thereby providing a sterilized material.

(Claims App., Br. 18; indentation, paragraphing, and emphasis added.)

The Examiner has maintained the following ground of rejection:⁴

Claims 1, 2, 6, 7, 9-14, and 32-37 stand rejected under 35 U.S.C. § 103(a) in view of the combined teachings of Hashizume⁵ and Hayakawa.⁶

Laugharn argues that the rejection should be reversed because Hashizume teaches effective sterilization only below -10°C and above 45°C, while Hayakawa teaches effective oscillating pressure sterilization only at temperatures well above 45°C, more specifically, at 70°C. (Br. 12; Reply 12-13.)

The Examiner maintains that it would have been obvious to apply the oscillating pressure techniques taught by Hayakawa to samples both at temperatures below -10°C and at temperatures between 40°C and 45°C. (FR 3; Ans. 4-5.)

⁴ Examiner's Answer mailed 24 June 2009 ("Ans.").

⁵ Chieko Hashizume et al., *Kinetic Analysis of Yeast Inactivation by High Pressure Treatment at Low Temperatures*, 59 Biosci. Biotech. Biochem. 1455 (1995).

⁶ I. Hayakawa et al., *Oscillatory Compared with Continuous High Pressure Sterilization on Bacillus stearothermophilus Spores*, 59 J. Food Sci. 164 (1994).

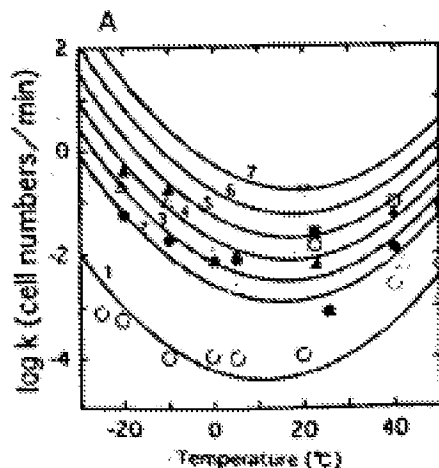
Because the preponderance of the evidence of record supports the Examiner's arguments for the range of 40°C to 45°C, we AFFIRM.

B. Discussion

Findings of fact throughout this Opinion are supported by a preponderance of the evidence of record.

Hashizume teaches the inactivation of yeast cells by applying static pressure at temperatures ranging from -20°C to 50°C. In Hashizume's words, referring to Fig. 2A, reproduced below, "[n]o or little inactivation was observed for the pressurization below 180 MPa⁷ at temperatures between 0°C and 40°C, but a rapid inactivation took place at 180 MPa when the temperature was above 45°C or below -10°C." (Hashizume at 1456, col. 1, 2d full para.) Figure 2A shows plots of rates of yeast inactivation as a function of temperature at pressures ranging from 0.1 MPa (1 atmosphere; curve 1 (○)) to 270 MPa (curve 7 (inverted open triangle)):

{Hashizume Figure 2A is shown below:}



{Figure 2A shows the temperature dependence of yeast inactivation}

⁷ 0.1 MPa = 1 atm = 1 bar (Spec. 11, ll. 21-23), so 180 MPa = 1800 atm.

Each curve shows the rate, k , of cell inactivation at a different pressure. As shown by curve 4 (\blacktriangle), at a pressure of 180 MPa, at 45°C, $\log k$ is about -1. As shown by curve 5, at a pressure of 210 MPa, a $\log k$ of -1 is obtained at a temperature of about 40°C. Moreover, at every pressure, the slope of the graph is positive between 40°C and 50°C, meaning that as the temperature rises from 40°C, the rate increases roughly exponentially.

As Laugharn points out (Reply 12)⁸, Hayakawa teaches killing bacteria spores by oscillatory pressurization (6 cycles, 5 min/cycle) to 400 MPa, the results being comparable to the application of continuous pressure at 600 MPa for 60 minutes. (Hayakawa 165, col. 2, 4th full para.; and Fig. 3.) Oscillatory pressurization to 600 MPa at 70°C reportedly resulted in complete sterilization. (*Id.*) Laugharn also points out (Reply 12; and 15, 1st para.), that Hayakawa indicates that the sterilizing effectiveness of oscillatory pressurization is due to “adiabatic explosion velocity of spore cell walls and high pressure water upon release of high pressures,” and because the “water permeability into the spore cell wall and spore protoplasm under high pressure were promoted by the rise in temperature (70°C).” (Hayakawa at 166, last para.) “Of course,” Hayakawa continues, “this temperature rise brought a viscosity drop of water from 0.95×10^{-3} Pa·sec (at 20°C) to 0.49×10^{-3} Pa·sec (at 70°C) and the water surface tension decreased from 72 dyne/cm (at 20°C) to 65 dyne/cm (at 70°C).” (*Id.* at 167, ll. 1-4.) Hayakawa concludes that “[t]hese physical

⁸ Although the Examiner indicated arguments in the Final Rejection (FR 3-4), specific claims were not identified until the Examiner’s Answer (Ans. 5-6). Under these circumstances, we do not consider Laugharn’s arguments in the Reply to be belated under 37 C.F.R. § 41.37(c)(1)(vii).

changes of water made the oscillatory pressurization more effective for destruction of spores.” (*Id.* at ll. 4-6.)

Laugharn’s argument that the skilled person would have understood Hayakawa “to require the high temperature (70 °C) to reduce the viscosity and surface tension of water to penetrate the cell wall” (Reply 15, 1st para.) is not well taken. Laugharn does not explain what in the passage cited would have taught persons having ordinary skill in the art that the effects of lowered viscosity and surface tension become important only at 70°C. On the contrary, the weight of the evidence is that the combined teachings of Hashizume and Hayakawa would have suggested that oscillatory pressurization would have increased the effectiveness of inactivation at all temperatures above 20°C, the more so as the temperature increased.

Laugharn argues further that “Hayakawa notes that oscillatory pressurization provides no sterilization advantage,” and that there is no distinction between continuous sterilization and oscillatory pressurization (Reply 15, last para.) because the same amount of sterilization was obtained by treatment for 60 min at 600 MPa and 70°C as with 6 cycles to 400 MPa at 70°C. These are, in Laugharn’s view, further reasons why the teachings of Hashizume and Hayakawa would not have been combined. We do not credit this argument because it overlooks the shorter time (6 cycles \times 5 min/cycle = 30 min) required for the oscillatory pressure assisted sterilization compared to the 60 minutes required by continuous pressurization to achieve the same degree of sterilization. The savings in

time, energy, and lessened exposure to potentially damaging temperatures all provide potential advantages of interest to the artisan.

Given the rapid rise in inactivation efficacy between 40°C and 50°C noted by Hashizume, and the mechanism of enhanced sterilization proposed by Hayakawa, we are not persuaded that the weight of the evidence is against the Examiner for the obviousness of oscillatory pressurization at temperatures between 40°C and 45°C, which is within the scope of claim 1.

The situation at temperatures below 0°C is different. Although Hashizume indicates that “[w]ater is in the form of liquid or Type I ice in these experiments, in which the sample is pressurized at sub-zero temperatures” (Hashizume 1456, last para., citation omitted), the Examiner has not come forward with evidence as to the state of water in yeast or other microorganisms at temperatures less than -10°C. Nor has the Examiner come forward with evidence from the prior art that there would have been any reason to apply oscillatory pressurization to frozen samples. We conclude, therefore, that Laugharn has shown harmful error, on the present record, in the Examiner’s rejection to the extent that the Examiner relies on the low temperature conditions described by Hashizume. However, for the reasons explained *supra*, such error is not fatal to the Examiner’s rejection.

With the exceptions of claims 9, 34, and 36, Laugharn does not raise arguments for the separate patentability of any claims. All other rejected claims therefore stand or fall with claim 1. 37 C.F.R. § 41.37(c)(1)(vii). Laugharn’s argument that the ten pressure cycles required by claim 9 would not have been obvious because Hayakawa teaches no more than six cycles (Reply 13) is without merit, as Laugharn fails to explain why a person

having ordinary skill in the art would not repeat pressure cycles until a desired degree of inactivation were obtained.

Regarding claim 34, Laugharn argues that because Hashizume teaches that proteins and lipids are damaged by high pressure, it would not have been obvious to maintain the biological activity of a macromolecule using methods requiring pressure cycles as taught by Hayakawa and as claimed. (Reply 13, penultimate para.) Laugharn also argues, however, that persons skilled in the art would not have had a reasonable expectation of successful sterilization of any organism, including viruses, as required by claim 36, because Hashizume teaches that different organisms have different sterilization characteristics. (Reply 14, 1st full para.) The application of pressure cycles would have required, in Laugharn's view, undue experimentation. (*Id.*)

These arguments regarding claim 34 and claim 36 are not persuasive because they are inconsistent and because they do not account for the level of ordinary skill in the art. First, the teachings of Hashizume that biological macromolecules such as proteins and lipids can be destroyed by pressure (Hashizume 1455, col. 1, 2d para.) would have indicated to the ordinary worker that viruses, which are comprised of proteins surrounding a nucleic acid core, and which in some instances further comprise lipids (e.g., so-called "enveloped" viruses, which have membranes (Spec. 19, l. 30, to 20, l. 4)), may be inactivated under sufficiently high pressures. Second, the concerns of Hashizume regarding the potential for lower temperature sterilization to preserve foods, and the major focus on the inactivation of cellular organisms, would have indicated to the ordinary worker that there

are situations in which inactivation or sterilization conditions should be kept as mild as possible. The teachings of Hayakawa regarding the cell-bursting effect of pressure changes would have further enhanced the “mild conditions” teachings of Hashizume, teaching the ordinary worker that inactivation or sterilization could be accomplished without destroying the biological activity of all biological macromolecules present in the sample, as required by claim 34.

Moreover, Laugharn has not directed our attention to credible supporting evidence in the record that the ordinary worker would have required undue experimentation to combine the teachings of Hashizume and Hayakawa while either preserving biological activities of desired macromolecules (claim 34) or while inactivating viruses (claim 36). The recognized “different responses” of different microorganisms to pressure and temperature would have led the ordinary worker to establish appropriate pressures, temperatures, and pressure cycles for the sample at hand. We also note Laugharn has not directed arguments towards the patentability of any claim that requires both the inactivation or sterilization of viruses and the preservation of biological activity of a macromolecule. We express no opinion as to whether processes of sterilizing viruses by pressure-cycle-enhanced sterilization while maintaining the biological activity of any particular macromolecule would have been obvious over the present record, as that question has not been placed before us. In any event, patentability cannot be based on limitations that are not express or inherent in a claim.

We conclude that Laugharn has failed to demonstrate harmful error in the Examiner’s rejections.

C. Order

We AFFIRM the rejection of claims 1, 2, 6, 7, 9-14, and 32-37 under 35 U.S.C. § 103(a) in view of the combined teachings of Hashizume and Hayakawa.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

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